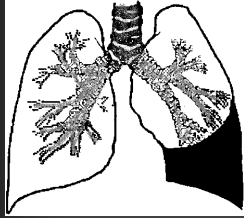


International Pleural Newsletter



A Publication of the International Pleural Network

Volume 8 Issue 2
April 2010

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Pleural Ultrasonography

Diagnosis of Malignant Pleural Effusion using Thoracic Ultrasound

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The most common cause of unilateral pleural effusions in the UK and USA is malignancy, with an estimated 250,000 new cases of malignant pleural effusions diagnosed annually¹. The gold standard imaging modality for patients with suspected malignant effusion is thoracic contrast-enhanced computed tomography (CECT) scanning. CECT is both a specific and a sensitive test for differentiating benign and malignant pleural disease².

Recently, an emerging role for thoracic ultrasound (TUS) in the investigation of malignant pleural effusion has been demonstrated. TUS is a quick, relatively inexpensive investigation, which is increasingly being performed by chest physicians. TUS is recognized as an accurate and reliable technique for pleural fluid detection, assessment of fluid characteristics and for guiding pleural intervention³.

More recently, TUS has been shown to be a valuable clinical tool in the diagnosis of malignant pleural effusion. Studies have evaluated high frequency real-time sonography in determining the nature of pleural effusions: appearances consistent with a high suspicion of malignancy include pleural thickening of more than 1 cm and the detection of pleural nodules⁴, but the sonographic fluid characteristics themselves are non-specific⁵.

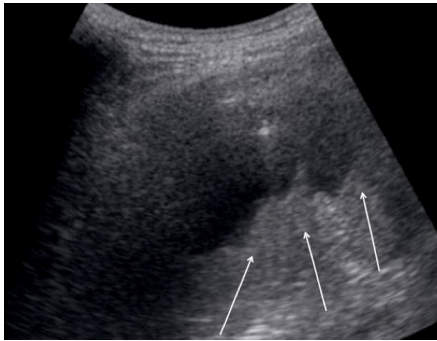
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The accuracy of TUS in the diagnosis of suspected malignant pleural effusion has been shown to be comparable to that of CECT⁶. In the study by Qureshi *et al.* TUS correctly diagnosed malignant pleural effusion with an overall sensitivity of 79%, specificity of 100%, positive predictive value (PPV) of 100% and negative predictive value of 73%. Good inter-observer agreement between TUS operators was also demonstrated⁶. This study used previously reported CECT morphological criteria for the diagnosis of malignant pleural disease² and applied them to TUS. These included: 1) diaphragmatic and parietal pleural nodule or nodules; 2) pleural thickening >1 cm (*below*); and 3) hepatic metastasis.

By employing a threshold value for parietal pleural thickening of >1 cm as suggestive of malignancy, TUS had a specificity of 95% and a PPV of 93% for



distinguishing malignant from benign disease⁶. The appearance of nodular pleural thickening on TUS was also associated with malignant pleural effusions and

demonstrated a specificity of 100% and a PPV of 100%⁶. The TUS echotexture of malignant pleural thickening appeared to be non-specific, and was hypoechoic, hyperechoic or isoechoic relative to the intercostal muscles. In contrast, TUS echotexture of benign pleural thickening was most often hypoechoic.

As well as the recognized CECT criteria, additional TUS morphological features were also shown to be associated with malignant pleural effusions, namely, visceral pleural thickening, diaphragmatic nodularity and thickness >7 mm (Table). In contrast, diaphragmatic thickening <5 mm and readily resolved normal diaphragmatic appearances, with all five layers clearly seen, were suggestive of benign disease⁶.

In summary, there are now defined TUS morphological features enabling the differentiation between benign and malignant pleural effusions. With its low cost and ready availability, TUS should be performed initially in the investigation of patients with pleural effusion of unknown etiology, with

CECT being reserved for patients requiring further investigation.

TUS morphological feature	Malignant pleural effusion	Benign pleural effusion
Parietal pleural thickening	>1 cm Non-specific echotexture	<1 cm Hypoechoic echotexture
Pleural nodularity/irregularity	Present	Absent
Visceral pleural thickening	Present	Absent
Diaphragmatic thickening	>7 mm	<7 mm
Diaphragmatic nodularity	Present	Absent
Hepatic metastasis	Present	Absent

1. American Thoracic Society. AJRCCM 2000; 162:1987-2001.
2. Leung AN, et al. AJR Am J Roentgenol 1990; 154:487-492.
3. Qureshi NR, et al. Clin Chest Med 2006; 27:193-213.
4. Yang PC, et al. AJR Am J Roentgenol 1992; 159:29-33.
5. Gorg C, et al. Eur Radiol 1997; 7:1195-1198.
6. Qureshi NR, et al. Thorax 2009; 64:139-143.

Ultrasound Guided Thoracentesis

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Approximately 1.5 million persons are found to have pleural effusions each year in the USA. Over the last several years, the use of portable, point of care ultrasound has greatly enhanced the evaluation and management of patients with pleural disease. Ultrasonography has been found to be more sensitive than chest X-ray for the detection of pleural fluid, can predict the need for more invasive pleural intervention and has been associated with a significant reduction in pneumothorax rates, when used to guide thoracentesis. Though there is a learning curve associated with the use of thoracic ultrasound (TUS), it is relatively short and should consist of both didactics as well as hands-on training^{1,2}.

Examination of the pleural space with ultrasound is best performed with a convex array 3.5 – 5MHz probe. This frequency range provides both excellent resolution and penetration. In the absence of pleural fluid, identification of the hyperechoic visceral and parietal pleurae can be difficult. However, when it is

present, evaluation of the pleural space, visceral and parietal pleura and even the lung becomes possible. Movement of the lung with respiration produces a 'sliding' or 'gliding' sign, and this dynamic movement identifies the visceral pleura and lung parenchyma. Diaphragmatic movement can also be visualized in real-time, and is a key reference point when starting to perform TUS examination of the pleural space.

Several studies have found that ultrasound can be helpful in identifying exudative pleural fluid. Complex effusions (either septated or non-septated) or homogeneously echoic effusions are always exudates. The converse, however, may not be true. Though transudates are almost always anechoic, anechoic fluid can be transudative or exudative.

Thoracentesis is typically thought to be a relatively safe procedure with few complications. The incidence of pneumothorax, however, has been reported to be as high as 20-39%. Though there are no blinded randomized trials comparing ultrasound vs physical exam guided thoracentesis, several studies have associated ultrasound use with lower complications. Procedural factors that have been shown to reduce the rate of pneumothorax include performance by experienced personnel³ as well as the use of ultrasound^{4,5}. Diacon's group found that, even in the hands of trained pulmonologists, the use of ultrasound increased the accuracy in site selection by 26%, and decreased the number of near misses (i.e. the number of potentially dangerous needle insertion sites) by 15% when compared to fluid localization by physical exam and chest radiography⁶. In a recent meta-analysis of 6,605 thoracenteses, Gordon *et al.* found that the use of ultrasound was associated with a 50% reduction in the risk of pneumothorax, using historical controls for comparative analysis³. In Mayo's study of critically ill patients receiving mechanical ventilation, the rate of pneumothorax using ultrasound-guided thoracentesis was 1.3%.

TUS has also been shown to be an excellent tool to both rule-out and in pneumothorax and is increasingly being used to evaluate lung parenchyma as well. Its use is quickly becoming the standard of care for procedural guidance in the pleural space.

1. Mayo PH, et al. Chest 2004; 125:1059-1062.
2. Mayo PH, et al. Chest 2009; 135:1050-1060.
3. Gordon CE, et al. Arch Intern Med 2010; 170:332-339.
4. Grogan DR, et al. Arch Intern Med 1990; 150:873-877.

5. Jones PW, et al. Chest 2003; 123:418-423.
6. Diacon AH, et al. Chest 2003; 123:436-441.

Ultrasound-Assisted Pleural Biopsies

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Recent studies have reemphasised the importance of transthoracic ultrasound (TUS) as a guide to pleural procedures, both with regards to safety and diagnostic yield. TUS is an ideal aid to the clinician, given its mobility, low cost, lack of irradiation, and short examination time. TUS is superior to chest radiography for the visualisation of pleural effusions. Moreover, the volume of fluid, the presence of septations, pleural thickening and pleural-based tumours can be accurately assessed.

Closed pleural biopsies were introduced in the late 1950s, and the Abrams, Cope or Vim-Silverman needles were used blindly for many decades. Unaided closed biopsies have a modest yield for malignancy, on the order of 60%. Tru-cut needle pleural biopsies were first performed in the 1980s, initially without TUS assistance. Maskell *et al.* showed that CT-guided Tru-cut pleural biopsies were superior for pleural malignancies compared to unaided Abrams needle biopsies (diagnostic yields 87% and 47% respectively)¹. Chang *et al.* previously found the diagnostic yield of TUS-guided Tru-cut pleural biopsy to be as high as 87% for all pleural pathologies (77% for malignancies)². For malignant mesothelioma our research has shown that this figure may be as high as 100%³.

In a recent prospective randomized study it was found that TUS-assisted Abrams needle biopsy specimens were more likely to contain pleural tissue than specimens obtained by means of TUS-assisted Tru-cut biopsies (91% vs 78.7%, $p=0.015$)⁴. Furthermore, Abrams needle biopsies had a significantly superior yield for pleural tuberculosis compared to Tru-cut needle biopsies (81.8% vs 65.2%, $p=0.022$), but not compared to previously reported figures for blind Abrams needle biopsies. The distribution of granulomatous inflammation in pleural tuberculosis is uniform over the pleura and visual aids, therefore, seem to offer little advantage

beyond increased safety. Interestingly, and contrary to previous reports, the respective yield for both needle types for pleural malignancies was comparable and relatively high, with TUS-assisted Abrams needle being diagnostic in 83.3%⁴. One possible explanation for this may have been the selection of low biopsy sites utilised, as the lower thoracic parietal pleura is more likely to contain secondary spread from visceral pleural metastases. Such an approach is possible with TUS assistance, but not with digital percussion as a guide. Moreover, malignant disease tends to give rise to more focal pleural involvement which may be visible on high frequency TUS (see article by Matin and Gleeson in this issue).

Apart from increasing diagnostic sensitivity, TUS very likely lowers the procedure-related risk. A recent survey carried out in the UK highlighted the dangers of blind pleural procedures: 67 of 101 trusts reported at least one serious complication from intercostal drainage (ICD)⁵. In all, 47 cases of serious lung or chest wall injuries with 8 deaths and 6 cases of ICD placement on the wrong side were described. Although similar multicenter data for unaided closed pleural biopsies does not exist, it seems plausible that similar complications can occur. Such incidents could be avoided by means of TUS assistance⁶.

In conclusion, we believe that closed pleural biopsies should routinely be performed under TUS guidance, as it is likely to increase the yield for malignancies and to decrease the risk of complications.

1. Maskell NA, et al. Lancet 2003; 361:1326-1330.
2. Chang BD, et al. Chest 1991; 100:1328-1333.
3. Diacon AH, et al. Respiration 2004; 71:519-522.
4. Koegelenberg CF, et al. Thorax 2010 (in press).
5. Harris A, et al. Postgrad Med J 2010; 86:68-72.
6. Diacon AH, et al. Chest 2003; 123:436-441.

Competence in Pleural Ultrasonography

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Ultrasonography has emerged as an important modality in the management of pleural diseases over the past decade. Routine use of ultrasonography for thoracentesis, pleural biopsy, placement of chest tubes and chronic indwelling pleural catheters lower the procedure risk and improves diagnostic accuracy. Reducing complications and improving diagnostic accuracy of pleura-related procedures have been the impetus' to mandate the routine use of ultrasound as the standard of care. However, formal training in the use of ultrasound has been adopted in a limited number of pulmonary/critical care programs in the United States.

The Critical Care Network of the American College of Chest Physicians and La Société de Réanimation de Langue Francaise collaborated in the development of a consensus statement on competence in critical care ultrasonography¹. Pleural ultrasonography was identified as one of the core areas in this statement. The proposed standard establishes the training goals needed for the non-radiologist to acquire competencies in pleural ultrasonography and is applicable outside the ICU environment.

The clinician must demonstrate competences in five areas according to the consensus document by: 1) having an understanding of basic ultrasound physics and how images are created through the interaction of sound waves and tissue; 2) demonstrating knowledge of the machine controls and transducer manipulation since they are personally conducting the exam; 3) being able to distinguish normal from abnormal ultrasound anatomy; 4) being able to interpret acquired images and know the limitations of ultrasonography pertinent to the examination conducted; and 5) being able to recognize when an examination is beyond the technical capabilities of either the device or themselves.

The elements required for mastery of pleural ultrasonography include: 1) identifying safe puncture sites and knowing how far to insert needles to avoid inadvertent penetration into lungs or other organs and vasculature; 2) identifying and characterizing pleural effusion echogenicity patterns such as anechoic, complex non-septate, complex septate, and homogenously complex; 3) identifying pleural effusion boundaries; 4) identifying the dynamic findings of pleural fluid, such as lung flaps, swirling

debris, and respirophasic shape changes; 5) identifying the liver, spleen, ascites, kidneys, heart, pericardium, aorta, and inferior vena cava; 6) providing a semi-quantitative assessment of pleural fluid volume; 7) identifying pleural-based masses and thickening; and 8) recognizing the technical limitations to image acquisition in the presence of subcutaneous emphysema, hemothorax, and echodense empyemas¹.

In our institution, new-trainees to our fellowship program spend the first week reviewing the basic ultrasound operations, understanding ultrasound probe manipulation, identifying landmarks above and below the diaphragm, and watching a 45-minute real-time video showing normal and abnormal pleural pathology. Image acquisition, transducer manipulation, and image interpretation is taught at bedside. In summary, competence can be easily obtained by those who are non-radiologically trained if a systematic approach is adopted.

1. Mayo PH, et al. Chest 2009; 135:1050-1060.

PLEURAL IMAGES

Pleural Metastases

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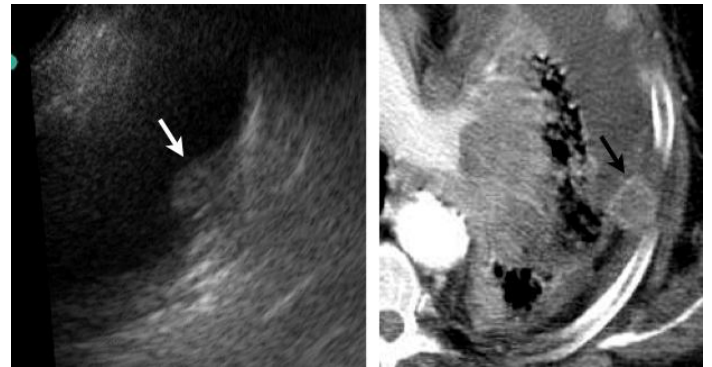
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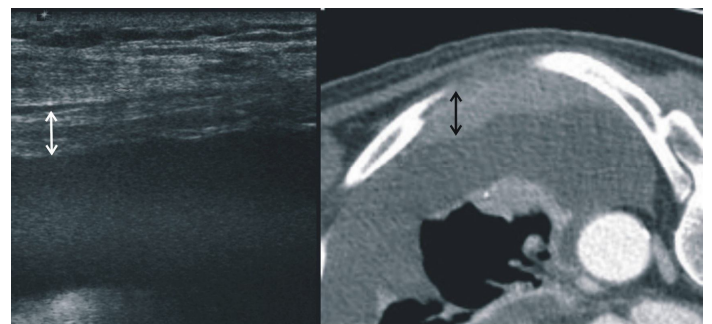
Case 1. An 80-year-old-man was hospitalized after a lung mass with an associated left pleural effusion was detected on a chest radiograph that was done to evaluate new-onset dyspnea on exertion. He had a 60-pack-year history of cigarette smoking. Thoracentesis yielded bloody fluid and analysis showed: erythrocyte count 250,000/ μ L, leukocytes 800/ μ L with 79% lymphocytes, total protein 3.9 g/dL, lactate dehydrogenase (LDH) 461 U/L, glucose 135 mg/dL, pH 7.44, adenosine deaminase (ADA) 18.4 U/L and positive cytology for an undifferentiated carcinoma. Immunoreactivity for thyroid transcription factor 1

(TTF-1) was negative in a cell block preparation of pleural fluid.

Both chest ultrasound and CT scanning revealed a moderate effusion along with multiple parietal pleural nodules (*below*) consistent with metastases. The CT images also indicated mediastinal lymph node and liver involvement from a primary lung tumor. Additional diagnostic maneuvers were considered unnecessary. The patient died two weeks later.



Case 2. An 89-year-old man was evaluated for a 3-month history of left scrotal swelling, growing lump in the upper back chest wall and progressive dyspnea. Chest ultrasound and CT exhibited parietal pleural thickening and effusion (*below*). Pleural fluid analyses showed: erythrocyte count 1010/ μ L, leukocytes 280/ μ L (99% lymphocytes), total protein 4 g/dL, LDH 636 U/L, glucose 117 mg/dL, pH 7.6, ADA 40.2 U/L, and negative cytological examination.



Biopsies of the parietal pleura (Tru-cut CT-guided), testicular mass and bone marrow were diagnostic of a diffuse large B-cell lymphoma. Staging also demonstrated chest wall, myocardial and abdominal lymph node involvement. The patient is currently receiving treatment with cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP).